Formulation and characterisation of Spironolactone- Eugenol-loaded LeciPlexes for topical delivery

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Background: Spironolactone (SP) is an inhibitor of androgen receptors, which has driven its use for treating androgen-related skin disorders such as acne. SP is used in particular to treat acne vulgaris (AV) owing to its ability to compete with androgens for sebocyte androgen binding sites that are found in the sebaceous glands. Thus, the interest in limiting the side effects of oral SP and improving efficacy supports the development of topical forms of SP. The drawbacks and limitations of using SP topically drove the development of novel drug delivery systems. The proposal was to design a dual drug delivery system of nanoparticles that includes SP associated with eugenol (EG). Various therapeutic benefits have been explored for EG, including anti-inflammatory, antioxidant, antimicrobial, etc. LeciPlexes (LPs) are an advanced liposome system first fabricated early in 2011 by Date, Nagarsenker et al. (2011).

Methods: Phospholipon 90 G (PL-90 G) was kindly gifted from Lipoid GmBH (Ludwigshafen, Germany). Spironolactone, Transcutol P, Eugenol, and Cetyl Trimethylammonium Bromide (CTAB). A single-step process produced LPs; the SP, CTAB, and PL-90 G were weighed and then solubilised in Transcutol P by using a water bath at 70 °C until a homogenous mixture was obtained. Then the distilled water at 70 °C was added to the blend with continuous magnetic stirring. EG was gradually added to the mix while stirring. The dialysis cassettes (MW of 10 kD) were used to calculate EE%. SP and EG were quantified using a newly proposed HPLC method.

Results: For data analysis purposes, 3-D response surface graphs were generated using the Minitab tool to assess the relationship strength between the independent and dependent variables in the SP-NPs formulation of the first phase experiment.

The ANOVA analysis indicated that both factors of PL-90G mM and the CTAB/PL-90G ratio had a significant effect on the PS and PDI at $p < 0.001$. The model lack of fit p-value was insignificant for PS and PDI, with $p = 0.081$ and $p = 0.130$, respectively. The EE% was over 80% for all SP-LP formulations, which indicates no remarkable differences were identified between the formulations. The ZP had positive charge and all formulations-maintained values greater than 40 mV. When EG was added, the XRD spectrum for the optimised formulation of SP and EG–loaded LP indicated an amorphous arrangement for SP. The EE% values of SP (86.1%) were almost the same for both optimised formulations.

Conclusions: The single-step method successfully fabricated the optimised LP formulation for topical delivery of SP and EG. It is supposed that SP and EG-loaded LPs could be promising carriers for targeting topical skin disorders such as acne.